High-Output Cardiac Failure Due to Hereditary Hemorrhagic Telangiectasia: A Case of an Extra-Cardiac Left to Right Shunt

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Abstract

High-output cardiac failure is a rare complication of hereditary hemorrhagic telangiectasia and can potentially be mistaken for other entities. We present a case of high-output cardiac failure because of large hepatic arteriovenous malformations, review the literature regarding the cardiac manifestations of the disease, and discuss the possible differential diagnoses.

Keywords

- hereditary hemorrhagic telangiectasia
- high-output cardiac failure
- Osler-Weber-Rendu
- arteriovenous malformation

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu syndrome, is an autosomal dominant systemic fibrovascular dysplasia characterized by mucocutaneous telangiectasias and arteriovenous malformations (AVMs).[1,2] A majority of causative genetic mutations in HHT arise from the endoglin (ENG) and activin-A receptor type-like kinase 1 (ACVRL1/ALK1) genes, which are responsible for growth factor receptors expressed on vascular endothelial cells. The receptors, when stimulated, lead to angiogenesis and repair.[2,3] The prevalence of HHT is reported to be between 1 in 5 to 10,000.[2,3] The diagnosis is confirmed when three of the four Curaçao criteria are present: (1) spontaneous recurrent epistaxis, (2) multiple telangiectasias at characteristic sites (lips, oral cavity, fingers, nose), (3) a first-degree relative with HHT, and (4) visceral AVMs (typically in the gastrointestinal [GI] tract, liver, lung, and brain).[1]

High-output cardiac failure (HOCF) is a rare complication of HHT.[4–6] In the liver, AVMs can be connections between the hepatic artery and portal vein, which manifest as portal hypertension, varices, or ascites. Alternatively, there can be connections between the hepatic artery and hepatic vein, manifesting as HOCF.[4] The pathogenesis of HOCF involves the shunting of oxygenated blood directly from the hepatic artery to the hepatic vein, thereby bypassing the liver and decreasing effective perfusion. The resulting increased oxygen demand and decreased systemic vascular resistance activate both the sympathetic nervous system and the renin-angiotensin-aldosterone system, causing greater cardiac output. Because of enhanced venous return over time, the right atrial pressure, pulmonary artery pressure, and left ventricular end-diastolic volume increase, thus causing left ventricular dilation and eventual cardiac failure.[7,8] HOCF in HHT has been linked to increased morbidity of the disease, including severity of epistaxis and transfusion requirement.[9,10]

Treatment for HHT includes supportive care, correction of iron deficiency anemia with intravenous iron and/or blood transfusions, endoscopic ablation, hepatic artery ligation,

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embolization, or banding, liver transplantation, and medical therapy with hormone therapy or bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor.[11,12] Conservative therapy with diuretics, antihypertensive agents, antiarrhythmic agents, and digoxin is the mainstay of treatment for HOCF.[7,8] In this article, we present a case of HOCF secondary to HHT, which is presented as atrial fibrillation.

Case Presentation

A 42-year-old Hispanic female patient with a history of monthly epistaxis and multiple episodes of GI bleeding causing iron deficiency anemia was transferred to our facility for dyspnea, new-onset atrial fibrillation, and concern for intra-cardiac left-to-right shunt. At an outside hospital, a right heart catheterization showed increased mixed venous oxygen saturation (Mv_{O_2}) of 90%. On examination, several telangiectasias were visible on the forehead, fingertips, and tongue (►**Fig. 1**). A grade IV/VI holosystolic murmur was audible throughout the precordium. The liver tip was palpable 6 cm below the costal margin and associated with a continuous bruit. Laboratory studies were significant for iron deficiency anemia, normal liver function tests, and normal INR (international normalized ratio).

Chest X-ray showed cardiomegaly and pulmonary vascular congestion (►**Fig. 2**). Transesophageal echocardiogram revealed mildly dilated left ventricle (LV), LV ejection fraction of 60%, moderately dilated right ventricle, severe biatrial dilation, severe tricuspid regurgitation because of tricuspid annular dilation, and severely increased pulmonary artery systolic pressure (80 mm Hg). No atrial septal defect (ASD), ventricular septal defect, patent ductus arteriosus, or other intra-cardiac shunt was identified. All four pulmonary veins drained into the left atrium. Examination of the liver during

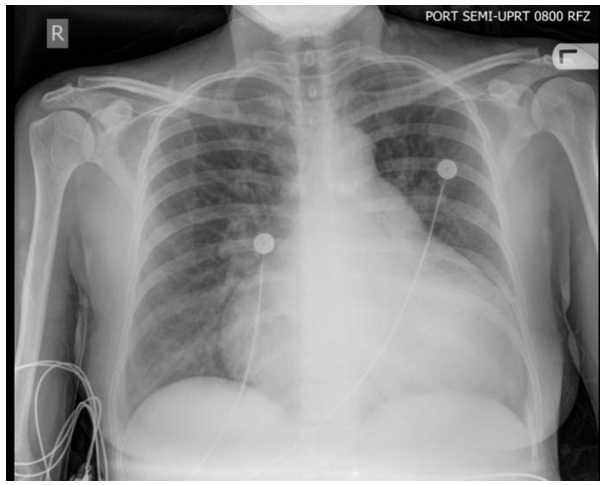

Fig. 2 Chest X-ray showing prominent cardiomegaly, pulmonary vascular congestion, and central prominence of the main pulmonary artery segment suggestive of pulmonary artery hypertension.

echocardiography revealed multiple, large arteriovenous (AV) fistulae with grossly increased flow in the celiac axis with a velocity of 4 m/s in systole and 1.7 m/s in end-diastole (►**Fig. 3**).

Right heart catheterization with serial oximetry measurements showed a significant elevation in all right-sided chambers and inferior vena cava (IVC) as compared with the superior vena cava (SVC) with an increased pulmonary blood flow to systemic blood flow ratio (Qp/Qs ratio) of 2.5 (►**Table 1**). Computed tomography angiography (CTA) of the abdomen showed diffuse AV shunting of bilateral lobes of an enlarged nodular liver, which was fed by a massive enlargement of the right and left hepatic arteries (►**Fig. 4**). The patient was treated conservatively with iron supplements to

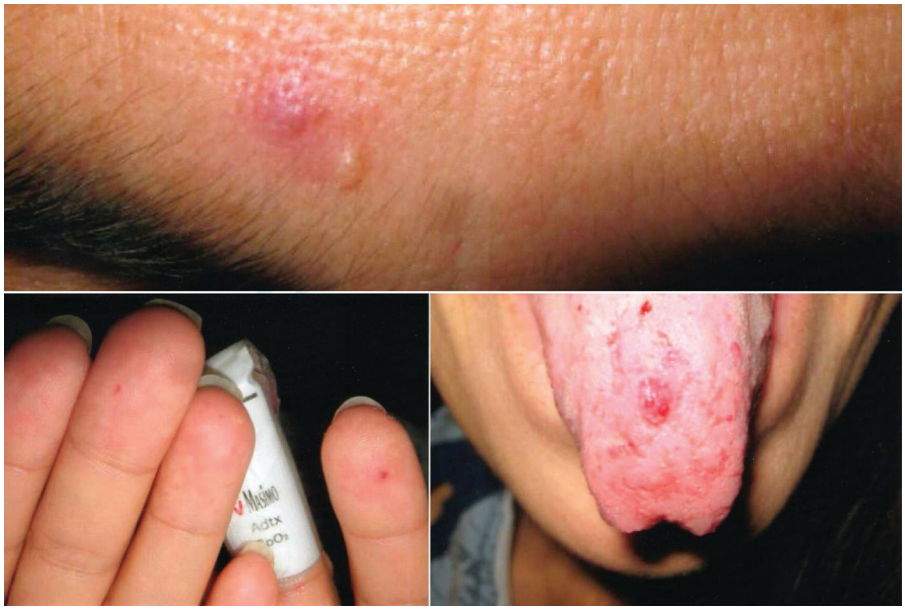

Fig. 1 Mucocutaneous telangiectasias on the forehead, fingers, and tongue.

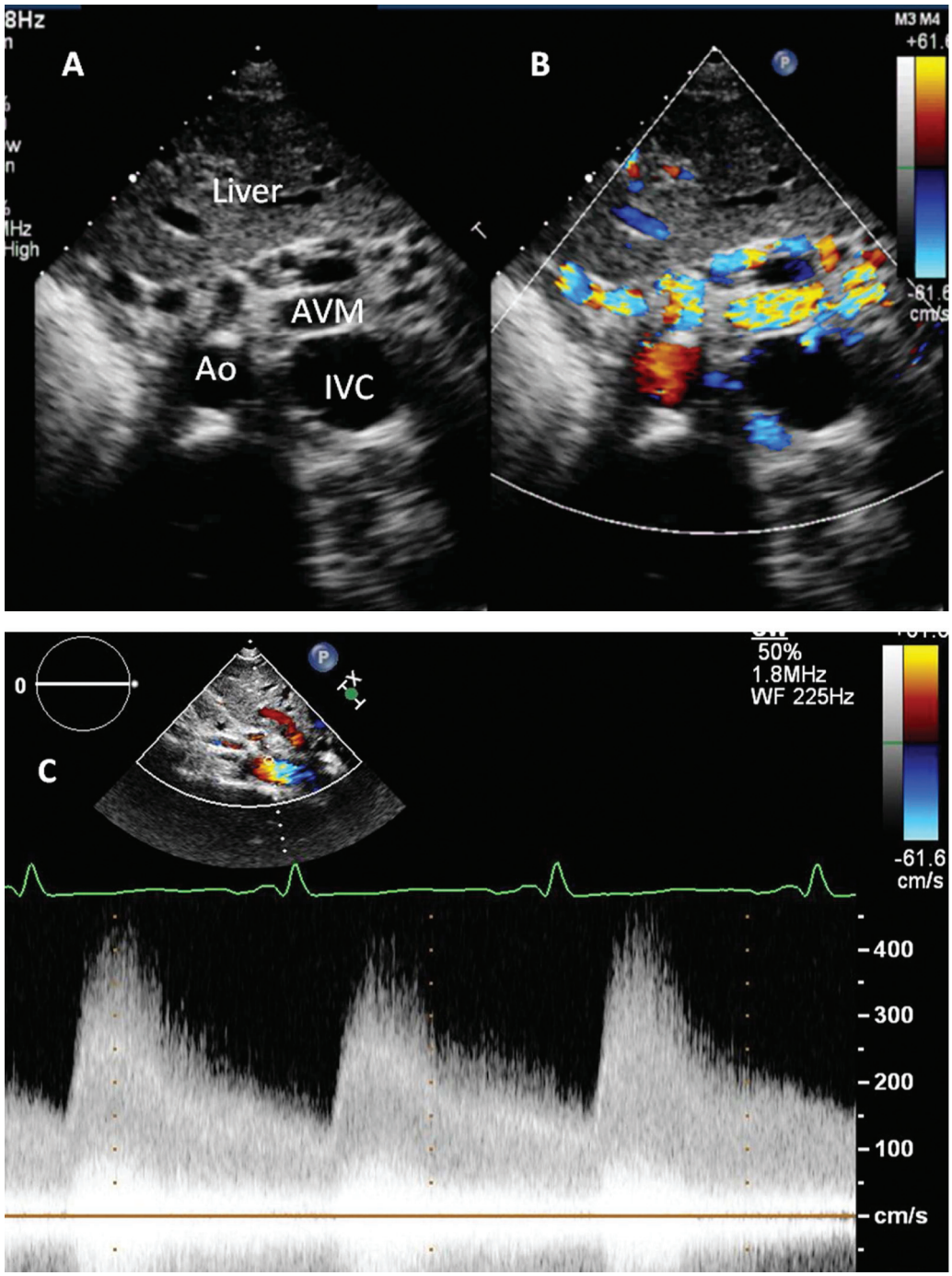

Fig. 3 Liver ultrasound demonstrating multiple, large arteriovenous fistulae (A and B) with grossly increased flow in the celiac axis (C).

combat the iron deficiency anemia produced by chronic GI blood loss.

Discussion

Our patient met three out of the four Curaçao criteria of HHT, as she presented a history of epistaxis, telangiectasias, and visceral AVMs. She also showed signs and symptoms of HOCF with evidence of intrahepatic shunting on imaging and pulmonary hypertension and left ventricular dilatation on echocardiogram. HOCF occurs most often in cases of HHT in which the shunt volume, the amount of arterial blood passing directly into the venous system via AVMs, exceeds 20% of the cardiac output.[4–6]

HOCF in HHT can masquerade as an intra-cardiac shunt at the level of the right atrium because of increased right-sided oxygen saturations inferior to the SVC. In our patient, the step-up in oxygen saturation occurred at the level of IVC below the diaphragm indicating a left-to-right shunt at the IVC level, which can occur in sinus venosus ASD of the IVC type and partial anomalous pulmonary venous drainage to the IVC or hepatic vein. However, these were ruled out by

Table 1 Right heart catheterization serial oximetry measurements

Site	Oxygen saturation (%)
Femoral artery	99
Pulmonary artery	86
High right atrium (RA)	84
Mid RA	86
Low RA	88
Right ventricle	85
Inferior vena cava	81
IVC (below diaphragm)	83
Superior vena cava (SVC)	61
High SVC	64
Low SVC	67

echocardiography, and hepatic AV fistulae were positively identified by ultrasound examination and CT scanning.

To differentiate an intra-cardiac shunt from a systemic, extra-cardiac shunt, a thorough history and physical examination should be performed. Symptoms of HOCF because of HHT include dyspnea on exertion, fatigue, and other classical components of the Framingham criteria. Diagnostic clues obtained from the personal or family history are key features of HHT. Physical examination findings suggestive of HOCF include a high-grade holosystolic murmur and a hepatic bruit.

On chest X-ray, in addition to the usual radiologic evidence of congestive heart failure, discrete pulmonary nodules with associated tubular opacities representing pulmonary AVMs can be seen. CT of the chest and abdomen may demonstrate vessels entering and exiting opacities in the lungs, suggestive of pulmonary AVMs, hepatomegaly, rapidly enhancing liver nodules, enlarged IVC, and early filling of hepatic or portal veins in the arterial phase.[13,14]

A high-output cardiac state is defined as one in which the cardiac index, cardiac output divided by total body surface area, exceeds 4 L/min/m^2 on right heart catheterization.[9] Apart from HHT, the differential diagnosis for HOCF also includes: AV fistula, chronic anemia, Paget disease, hyperthyroidism, thiamine deficiency, obesity, and carcinoid syndrome.[15] More than 113 cases of HOCF caused by HHT have been presented in the literature, mostly in the form of case reports, case series, and cross-sectional studies, as well as one case-control study.[4–9,13]

Conclusion

It is important to diagnose HOCF in the setting of HHT. The underlying disease is not intrinsic cardiac pathology, but peripheral tissue hypoxemia secondary to hepatic vascular malformation which requires a different approach to intervention and long-term monitoring.

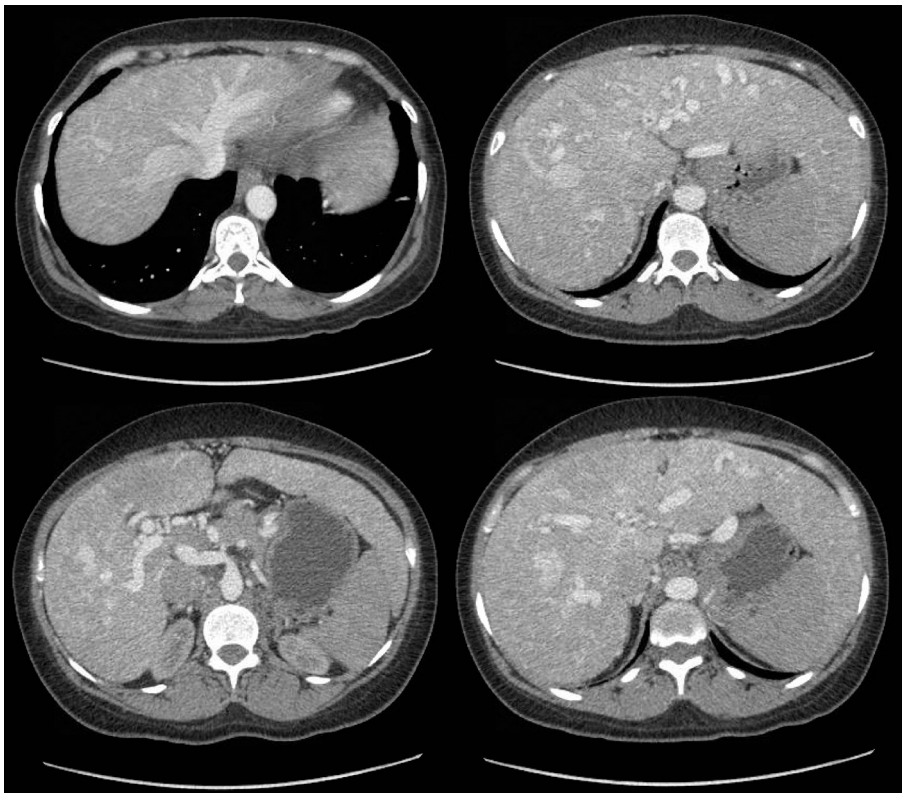

Fig. 4 Computed tomography of the abdomen with contrast demonstrating severely enlarged nodular liver with several irregular vascular channels connecting dilated hepatic vessels.

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